To: Kingshuk Das[kdas@theranos.com]; Donald Tschirhart[dtschirhart@theranos.com]; Daniel Young[dyoung@theranos.com];
'David Zifkin'[dzifkin@BSFLLP.com]
Cc: Sunny Balwani[sbalwani@theranos.com]
From: Tina Lin
Sent: Fri 3/25/2016 7:23:39 PM
Importance: Normal
Subject: RE: XPT 10x flags
Received: Fri 3/25/2016 7:23:40 PM
D5421_2_D5423.docx

Thanks King!

We did do #1.

I'm working on finishing #2 now.

#3 was also already done, per the instructions in the attachment you sent me.

Thanks,

Tina

From: Kingshuk Das
Sent: Friday, March 25, 2016 11:22 AM
To: Tina Lin <tlin@theranos.com>; Donald Tschirhart <dtschirhart@theranos.com>; Daniel Young <dyoung@theranos.com>; 'David Zifkin' <dzifkin@BSFLLP.com>
Cc: Sunny Balwani <sbalwani@theranos.com>
Subject: Re: XPT 10x flags

I just spoke with Jen, and got clarity on what she and Fran did, which is not what is referenced below.

I'll make the re-analysis very simple, not only because it makes it correct, but also much quicker (because these reports need to go out ASAP, to get read/receipt for Monday submission):

For every analysis that we are submitting this round:

1. VOID every run that fails Theranos-established QC rules [should already be done]
2. VOID every run where ANY QC value falls outside MANUFACTURER RECOMMENDED RANGE (based on package insert target and acceptable range)

3. VOID every "abnormal" month of patient results that were flagged by myself or others as deviating significantly from "normal" months--this list of months is in separate email(s) to Tina [should already be done]

The reason why I'm leaving out the 10x rule is that approach #2 catches every single QC that falls outside manufacturer rec's--the rational application of the 10x rule, based on past practices/data is not feasible right now. We can state that 10x rule was used as a warning, but not followed-up properly--it's the truth, but doesn't help the case.

Thanks,

king

—

From: Kingshuk Das
Sent: Friday, March 25, 2016 8:53 AM
To: Tina Lin; Donald Tschirhart; Daniel Young; 'David Zifkin'

Confidential   THPFM0005487131

Fantastic--that means some of the runs you flagged during 10x analysis were already voided?

Re: sodium, you'll have to explain what the adjustments were, and why--then I'll let you know how to deal with those

Better to discuss when I get there

I'll stop by,

k

From: Tina Lin
Sent: Friday, March 25, 2016 8:14 AM
To: Kingshuk Das; Donald Tschirhart; Daniel Young; 'David Zifkin'
Cc: Sunny Balwani
Subject: RE: XPT 10x flags

Hey King,

We already went through the exercise for flagging whenever our lab range exceeds manufacturer's range and void runs where QCs fall outside manufacturer's range – that's what Jen and Martha already did in round 1.

Let me know once you've gotten a chance to read my notes regarding Sodium below.

Thanks!

-Tina

From: Kingshuk Das
Sent: Friday, March 25, 2016 8:07 AM
To: Tina Lin <tlin@theranos.com>; Donald Tschirhart <dtschirhart@theranos.com>; Daniel Young <dyoung@theranos.com>; 'David Zifkin' <dzifkin@BSFLLP.com>
Cc: Sunny Balwani <sbalwani@theranos.com>
Subject: Re: XPT 10x flags

Also, related note: this approach (using manufacturer rec'd ranges) should be used for every QC data set we intent on submitting for patient impact analysis--i.e. whenever our lab range exceeds manufacturer's range, void runs where QC's fall outside manufacturer rec's--have to be consistent across all our analyses, good practice, but also will keep us from getting dinged for not doing it.

-k

From: Kingshuk Das
Sent: Friday, March 25, 2016 8:01 AM
To: Tina Lin; Donald Tschirhart; Daniel Young; 'David Zifkin'
Cc: Sunny Balwani
Subject: Re: XPT 10x flags

Actually, let me make it easier for you...was just going to email you regarding all these analyses anyway.

I was looking over the 10x excel sheets again, based on last night's discussion, and noticed something I missed the first go-around: the laboratory appears to have concocted (based on my assumption that "calculated mean" = empirical (based on day-to-day operation of methods) QC target means/ranges in some cases FAR outside what would likely be recommended by manufacturer's package insert for those lots. That is also deficient QC because those manufacturer rec's are already intentionally broadened to support all laboratories/operators/etc.

Tina, in addition to any sets of runs we flagged--for any reason (to answer your question below, any QC level fail = fail, regardless of where it falls in respect to patient distributions, cannot predict effect on human matrix)--void all runs with QC target means/ranges outside manufacturer's package insert rec's. At a glance, it looks like it only applies to certain analytes during certain time periods--where, as you say, there were mean adjustments for whatever (probably no good) reason. Ironically, it might be the case that when you use manufacturer recommended means/targets, may negate some/many of the 10x violations--so they may balance out.

I'll be in fairly soon, so stop by if you have any Q's.

Sorry for missing this...but is very important to get correct since we'll be sending in supporting documentation.

Thanks,

king

From: Tina Lin
Sent: Friday, March 25, 2016 4:39 AM
To: Kingshuk Das; Donald Tschirhart; Daniel Young; 'David Zifkin'
Cc: Sunny Balwani
Subject: RE: XPT 10x flags

King,

An update on the two analytes that had impact for 1800s based on your 10x review. Action requested highlighted inred.

ALT

- 1798 patient results on the dates you flagged

- 148 of these were close to the levels you flagged

    - As an example, levels 2 and 3 were 10x-flagged, but there were **no** 10x issues for level 1. This count of 148 results does not count results that are closer to levels without 10x issues.

- Please advise which of the above (1798 or 148) you'd like to void.

Sodium

- Sodium's calculated means for all levels were skewed due to an adjustment during dilution testing period in March-May 2015. That's why you were seeing the wacky numbers.

- I've re-reviewed LJ plots for all testing periods to identify potential 10x's and found the following in 2015 (no 10x in 2014 on testing days):

  o ADVIA 1

    ▪ 4/27 L3 (within 1 SD)

    ▪ June all levels (though this seems to be due to a bad adjustment of mean based on previous month's QCs – QC looks acceptable otherwise)

    ▪ 7/11-7/12 L3 (within 1 SD)

    ▪ 7/29-7/30 L3

  o ADVIA 2

    ▪ 5/7 L1,3

    ▪ 5/8-5/10 L3

    ▪ June all levels (again, like ADVIA 1, looks to be an issue with adjustment of mean, not actual runs)

    ▪ Late September L3 (this is on a new lot, looks like L3 mean was not properly established)

  o ADVIA 3

    ▪ 1/12-1/13 L1 (within 0.5 SD)

- Can you highlight which of the above dates you'd like to void, or I can bring over the binders in the morning for you to review as well?ADVIA 3 looks really good for example, a 10x shift was barely noticeable...

Thanks,

Tina

From: Kingshuk Das
Sent: Thursday, March 24, 2016 8:56 PM
To: Tina Lin <tlin@theranos.com>; Donald Tschirhart <dtschirhart@theranos.com>; Daniel Young <dyoung@theranos.com>
Cc: Sunny Balwani <sbalwani@theranos.com>
Subject: Re: XPT 10x flags

Should apply to all sections--the bias corrections we're adding just aren't defensible.

Was trying to write up one of them just now--frankly speaking, it has no scientific/medical merit...was just being done to artificially decrease number of accessions, which is far from sound sound medical practice

Tina, this will be a pain, but please go back and remove the biases we applied via months of "normal" patient distributions vs. "biased/shifted" patient distributions...for a number of analytes. We were just voiding those patients where the flags changed, but cannot defend that practice in our response. We need to void those entire shifted distributions because, as we discussed around and around before, we cannot predict magnitude of bias in these situations (we're just able to detect high likelihood of bias, probably mostly preanalytical, but maybe other elements).

Sorry to dump all this tonight, but it was so painfully obvious when I went back to patient assessments.

Thanks,

king

From: Tina Lin
Sent: Thursday, March 24, 2016 8:17 PM
To: Kingshuk Das; Donald Tschirhart; Daniel Young
Cc: Sunny Balwani
Subject: RE: XPT 10x flags

Ah, that was the direction from Daniel's third, assumed it was similar for yours. I'll redo your section... just a moment.

 Thanks,

Tina

From: Kingshuk Das
Sent: Thursday, March 24, 2016 8:16 PM
To: Tina Lin <tlin@theranos.com>; Donald Tschirhart <dtschirhart@theranos.com>; Daniel Young <dyoung@theranos.com>
Cc: Sunny Balwani <sbalwani@theranos.com>
Subject: Re: XPT 10x flags

 Just read this email more carefully--that's the incorrect analysis

 We're not applying bias and just voiding reports which change flags--ALL affected patients are to VOIDED

 Sorry if there was confusion, but I don't remember giving this order.

 Thanks,

king

From: Tina Lin
Sent: Thursday, March 24, 2016 11:40 AM
To: Donald Tschirhart; Kingshuk Das; Daniel Young
Cc: Sunny Balwani
Subject: XPT 10x flags

Hi all,

 I'm attaching the list of albumins and TPs that had changed flags due to 10x analysis. Can you confirm this is what you want? There are ~800 results, half and half TP/Alb. (We originally flagged 187 ALB, 61 TP.) Please review whether all flag changes are significant (e.g. are H to N or N to H flag changes for protein significant?).

 With this, and King's Troponin (~9 patients total) analysis, we'll finally be completed with our venous analysis.

 Thanks,

Tina